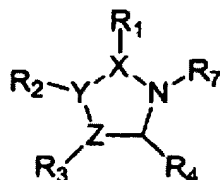


Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application.

Listing of Claims:

1 1. (Currently amended) A method of modulating an Edg-7 receptor mediated
2 biological activity comprising contacting a cell expressing the Edg-7 receptor with an amount of
3 ~~an~~ a modulator of the Edg-7 receptor sufficient to modulate the Edg-7 receptor mediated
4 biological activity wherein the modulator is a compound of the ~~structural formula~~ Formula (I):



(I)

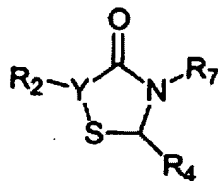
7 or a pharmaceutically ~~available~~ acceptable solvate or hydrate thereof, wherein;

8 each of R₁, R₂, R₃, R₄ and R₇ is absent or independently selected from -H, -halo, -NO₂,
9 -CN, -C(R₅)₃, -(CH₂)_mOH, -N(R₅)(R₅), -O(CH₂)_mR₅, -C(O)R₅, -C(O)NR₅R₅,
10 -C(O)NH(CH₂)_m(R₅), -OCF₃, -benzyl, -CO₂CH(R₅)(R₅), -(C₁-C₁₀)alkyl,
11 -(C₂-C₁₀)alkenyl, -(C₂-C₁₀)alkynyl, -(C₃-C₁₀)cycloalkyl, -(C₈-C₁₄)bicycloalkyl,
12 -(C₅-C₁₀)cycloalkenyl, -(C₅)heteroaryl, -(C₆)heteroaryl, -(C₅-C₁₀)heteroaryl,
13 -naphthyl, -(C₃-C₁₀)heterocycle, -CO₂(CH₂)_mR₅, -N(OH)aryl, -NHC(O)R₅,
14 -NHC(O)OR₅, -NHC(O)NHR₅, ~~heterocycloalkyl~~ heterocycloalkyl,
15 -C(S)N(R₅)(R₅), -(C₁-C₁₀)alkylNHC(O)(CH₂)_mR₅, -(C₁-C₁₀)alkylNR₅R₅,
16 -OC(O)(CH₂)_mCHR₅R₅, -CO₂(CH₂)_mCHR₅R₅, -OC(O)OR₅, -SR₅, -S(O)R₅,
17 -S(O)₂R₅, -S(O)₂NHR₅, ~~or~~ and



each R₅ and R₆ is independently selected from -H, -halo, -NO₂, -CN, -OH,
-CO₂H, -N(C₁-C₁₀)alkyl(C₁-C₁₀)alkyl, -O(C₁-C₁₀)alkyl,
-C(O)(C₁-C₁₀)alkyl, -C(O)NH(CH₂)_m(C₁-C₁₀)alkyl, -OCF₃, -benzyl,
-CO₂(CH₂)_mCH((C₁-C₁₀)alkyl(C₁-C₁₀)alkyl), -CO₂(C₁-C₁₀)alkyl,
-(C₁-C₁₀)alkyl, -(C₂-C₁₀)alkenyl, -(C₂-C₁₀)alkynyl, -(C₃-C₁₀)cycloalkyl,
-(C₈-C₁₄)bicycloalkyl, -(C₅-C₁₀)cycloalkenyl, -(C₅)heteroaryl,
-(C₆)heteroaryl, -phenyl, naphthyl, -(C₃-C₁₀)heterocycle,
-CO₂(CH₂)_m(C₁-C₁₀)alkyl, -CO₂(CH₂)_mH, -NHC(O)(C₁-C₁₀)alkyl,
-NHC(O)NH(C₁-C₁₀)alkyl, -NH(aryl), -N=C(aryl),
-OC(O)O(C₁-C₁₀)alkyl, ~~or~~ and -SO₂NH₂;
X, Y, and Z are each independently selected from C=O, O, S, C, ~~or~~ and N; wherein if X,
Y, or Z is O or S, R₁ is an electron pair;
R₁, R₂, R₃, R₄ and R₇ taken in any combination can form one or more substituted or
unsubstituted 5 or 6 membered cyclic or heterocyclic rings or a 6-membered
aromatic ring;
two R₆ groups on adjacent carbon atoms can together form a 5 or 6 membered cyclic or
heterocyclic ring or a 6-membered aromatic ring;
each m is independently an integer ranging from 0 to 8; and
each p is independently an integer ranging from 0 to 5.

2. (Currently amended) A method of modulating an Edg-7 receptor mediated
biological activity in a subject comprising administering to the subject a therapeutically effective
amount of a modulator of the Edg-7 receptor wherein the modulator is a compound of ~~the~~
~~structural formula~~ Formula (II):



(II)

or a pharmaceutically ~~available~~ acceptable solvate or hydrate thereof, wherein;

each of R_1 , R_2 , R_3 , R_4 and R_7 is absent or independently selected from -H, -halo, -NO₂,
-CN, -C(R₅)₃, -(CH₂)_mOH, -N(R₅)(R₅), -O(CH₂)_mR₅, -C(O)R₅, -C(O)NR₅R₅,
-C(O)NH(CH₂)_m(R₅), -OCF₃, -benzyl, -CO₂CH(R₅)(R₅), -(C₁-C₁₀)alkyl,
-(C₂-C₁₀)alkenyl, -(C₂-C₁₀)alkynyl, -(C₃-C₁₀)cycloalkyl, -(C₈-C₁₄)bicycloalkyl,
-(C₅-C₁₀)cycloalkenyl, -(C₅)heteroaryl, -(C₆)heteroaryl, -(C₅-C₁₀)heteroaryl,
-naphthyl, -(C₃-C₁₀)heterocycle, -CO₂(CH₂)_mR₅, -N(OH)aryl, -NHC(O)R₅,
-NHC(O)OR₅, -NHC(O)NHR₅, ~~heterocycloalkyl~~ heterocycloalkyl,
-C(S)N(R₅)(R₅), -(C₁-C₁₀)alkylNHC(O)(CH₂)_mR₅, -(C₁-C₁₀)alkylNR₅R₅,
-OC(O)(CH₂)_mCHR₅R₅, -CO₂(CH₂)_mCHR₅R₅, -OC(O)OR₅, -SR₅, -S(O)R₅,
-S(O)₂R₅, -S(O)₂NHR₅, \emptyset and



each R₅ and R₆ is independently selected from -H, -halo, -NO₂, -CN, -OH,
-CO₂H, -N(C₁-C₁₀)alkyl(C₁-C₁₀)alkyl, -O(C₁-C₁₀)alkyl, -C(O)
(C₁-C₁₀)alkyl, -C(O)NH(CH₂)_m(C₁-C₁₀)alkyl, -OCF₃, -benzyl,
-CO₂(CH₂)_mCH((C₁-C₁₀)alkyl(C₁-C₁₀)alkyl), -CO₂(C₁-C₁₀)alkyl,
-(C₁-C₁₀)alkyl, -(C₂-C₁₀)alkenyl, -(C₂-C₁₀)alkynyl, -(C₃-C₁₀)cycloalkyl,
-(C₈-C₁₄)bicycloalkyl, -(C₅-C₁₀)cycloalkenyl, -(C₅)heteroaryl,
-(C₆)heteroaryl, -phenyl, naphthyl, -(C₃-C₁₀)heterocycle,
-CO₂(CH₂)_m(C₁-C₁₀)alkyl, -CO₂(CH₂)_mH, -NHC(O)(C₁-C₁₀)alkyl,
-NHC(O)NH(C₁-C₁₀)alkyl, -NH(aryl), -N=C(aryl),
-OC(O)O(C₁-C₁₀)alkyl, \emptyset and -SO₂NH₂;

X, Y, and Z are each independently selected from C=O, O, S, C, \emptyset and N; wherein if X,
Y, or Z is O or S, R₁ is an electron pair;

31 R₁, R₂, R₃, R₄ and R₇ taken in any combination can form one or more substituted or
32 unsubstituted 5 or 6 membered cyclic or heterocyclic rings or a 6-membered
33 aromatic ring;
34 two R₆ groups on adjacent carbon atoms can together form a 5 or 6 membered cyclic or
35 heterocyclic ring or a 6-membered aromatic ring;
36 each m is independently an integer ranging from 0 to 8; and
37 each p is independently an integer ranging from 0 to 5.

1 3. (Original) The method of Claim 1 or 2, wherein the modulator is an agonist.

1 4. (Original) The method of Claim 1 or 2, wherein the modulator is an antagonist.

1 5. (Original) The method of Claim 1 or 2, wherein the modulator exhibits at least
2 about 200 fold inhibitory selectivity for Edg-7 relative to other Edg receptors.

1 6. (Original) The method of Claim 1 or 2, wherein the modulator exhibits at least
2 about 40 fold inhibitory selectivity for Edg-7 relative to other Edg receptors.

1 7. (Original) The method of Claim 1 or 2, wherein the modulator exhibits at least
2 about 12 fold inhibitory selectivity for Edg-7 relative to other Edg receptors.

1 8. (Original) The method of Claim 1 or 2, wherein the modulator exhibits at least
2 about 5 fold inhibitory selectivity for Edg-7 relative to other Edg receptors.

1 9. (Original) The method of Claim 1 or 2, wherein the modulator exhibits at least
2 about 20 fold inhibitory selectivity for Edg-7 relative to other Edg receptors.

1 10. (Original) The method of Claim 1 or 2, wherein the modulator exhibits at least
2 about 200 fold inhibitory selectivity for Edg-7 relative to Edg-4 and Edg-2 receptors.

1 11. (Original) The method of Claim 1 or 2, wherein the modulator exhibits at least
2 about 40 fold inhibitory selectivity for Edg-7 relative to Edg-4 and Edg-2 receptors.

1 **12.** (Original) The method of Claim 1 or 2, wherein the modulator exhibits at least
2 about 12 fold inhibitory selectivity for Edg-7 relative to Edg-4 and Edg-2 receptors.

1 **13.** (Original) The method of Claim 1 or 2, wherein the modulator exhibits at least
2 about 5 fold inhibitory selectivity for Edg-7 relative to Edg-4 and Edg-2 receptors.

1 **14.** (Original) The method of Claim 1 or 2, wherein the biological activity is cell
2 proliferation.

1 **15.** (Original) The method of Claim 14, wherein the modulator exhibits at least about
2 200 fold inhibitory selectivity for Edg-7 relative to other Edg receptors.

1 **16.** (Original) The method of Claim 14, wherein the modulator exhibits at least about
2 5 fold inhibitory selectivity for Edg-7 relative to other Edg receptors.

1 **17.** (Original) The method of Claim 14, wherein the modulator exhibits at least about
2 200 fold inhibitory selectivity for Edg-7 relative to Edg-4 and Edg-2 receptors.

1 **18.** (Original) The method of Claim 14, wherein the modulator exhibits at least about
2 5 fold inhibitory selectivity for Edg-7 relative to Edg-4 and Edg-2 receptors.

1 **19.** (Original) The method of Claim 14, wherein cell proliferation leads to ovarian
2 cancer, peritoneal cancer, endometrial cancer, cervical cancer, breast cancer, colon cancer or
3 prostrate cancer.

1 **20.** (Original) The method of Claim 14, wherein cell proliferation is stimulated by
2 LPA.

1 **21.** (Original) The method of Claim 1 or 2, wherein the biological activity is calcium
2 mobilization, VEGF synthesis, IL-8 synthesis, platelet activation, cell migration,
3 phosphoinositide hydrolysis, inhibition of cAMP formation, actin polymerization, apoptosis,

angiogenesis, inhibition of wound healing, inflammation, cancer invasiveness, suppressing autoimmune responses, or atherogenesis.

22. (Original) The method of Claim 1 or 2 wherein the modulator binds to the Edg-7 receptor with a binding constant of at least about 10 nM.

23. (Original) The method of Claim 1 or 2 wherein the modulator binds to the Edg-7 receptor with a binding constant between about 1 μ M and 100 fM.

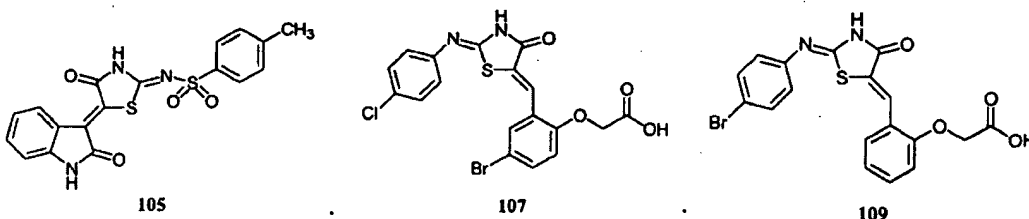
24. (Original) The method of Claim 1 or 2, wherein the modulator is a nucleic acid, protein or carbohydrate.

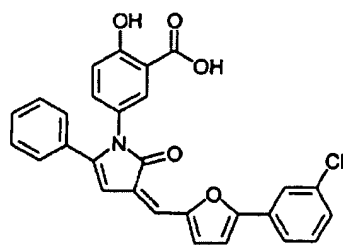
25. (Original) The method of Claim 1 or 2, wherein the modulator is an organic molecule of molecular weight of less than 750 daltons.

26. (Original) The method of Claim 1, wherein the cell is a hepatoma cell, an ovarian cell, an epithelial cell, a fibroblast cell, a neuronal cell, a carcinoma cell, a pheochromocytoma cell, a myoblast cell, a platelet cell or a fibrosarcoma cell.

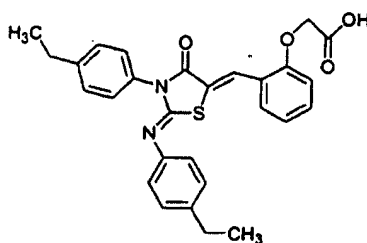
27. (Original) The method of Claim 21, wherein the cell is OV202 human ovarian cell, a HTC rat hepatoma cell, a CAOV-3 human ovarian cancer cell, MDA-MB-453 breast cancer cell, MDA-MB-231 breast cancer cell, HUVEC cells A431 human epitheloid carcinoma cell or a HT-1080 human fibrosarcoma cell.

28. (Currently amended) The method of Claim 1 or 2 wherein the modulator has ~~a the~~ following structural formula selected from:

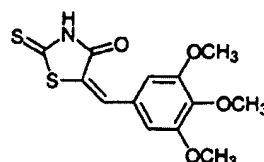




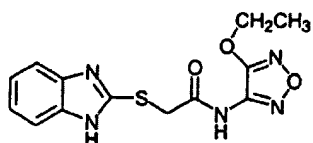
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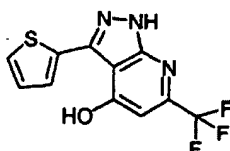
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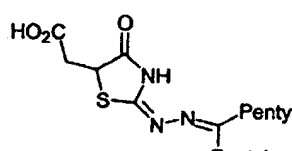
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123



125



127

and

29. (Currently amended) A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases in a patient in need of said treatment or said prevention, said method comprising administering to a said patient in need of such treatment or prevention a therapeutically effective amount of a compound of ~~structural formula~~ Formulae (I) or (II).

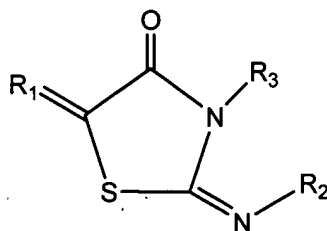
30. (Currently amended) A method for treating or preventing ovarian cancer, peritoneal cancer, endometrial cancer, cervical cancer, breast cancer, colorectal cancer, uterine cancer, stomach cancer, small intestine cancer, thyroid cancer, lung cancer, kidney cancer, pancreas cancer, ~~prostrate~~ prostate cancer, adult respiratory distress syndrome (ARDS), asthma, transcorneal freezing, cutaneous burns, ischemia or ~~artherosclerosis~~ atherosclerosis in a patient in need of said treatment or said prevention, said method comprising administering to a said patient in need of such treatment or prevention a therapeutically effective amount of a compound of ~~structural formula~~ Formulae (I) or (II).

31. (Currently amended) A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases in a patient in need of said treatment or said prevention, said method

comprising administering to a said patient in need of such treatment or prevention a therapeutically effective amount of a compound of ~~structural formula~~ Formulae (I) or (II) and one or more agonists or antagonists of an Edg-7 receptor.

32. (Currently amended) A method for treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases in a patient in need of said treatment or said prevention, said method comprising administering to a said patient in need of such treatment or prevention a therapeutically effective amount of a compound of structural formula (I) or (II) and one or more drugs useful in treating or preventing cancers, acute lung diseases, acute inflammatory exacerbation of chronic lung diseases, surface epithelial cell injury, or cardiovascular diseases.

33. (New) A method of treating cancer in a patient comprising:
administering to the patient a therapeutically effective amount of a modulator of an Edg-7 receptor wherein the modulator is a compound of Formula (III):

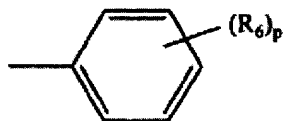


(III)

or a pharmaceutically available solvate or hydrate thereof, wherein

R₁, R₂ and R₃ are independently selected from -H, -halo, -NO₂, -CN, -C(R₅)₃, -(CH₂)_mOH, -N(R₅)(R₅), -O(CH₂)_mR₅, -C(O)R₅, -C(O)NR₅R₅, -C(O)NH(CH₂)_m(R₅), -OCF₃, -benzyl, -CO₂CH(R₅)(R₅), -(C₁-C₁₀)alkyl, -(C₂-C₁₀)alkenyl, -(C₂-C₁₀)alkynyl, -(C₃-C₁₀)cycloalkyl, -(C₈-C₁₄)bicycloalkyl, -(C₅-C₁₀)cycloalkenyl, -(C₅)heteroaryl, -(C₆)heteroaryl, -(C₅-C₁₀)heteroaryl, -naphthyl, -(C₃-C₁₀)heterocycle, -CO₂(CH₂)_mR₅, -N(OH)aryl, -NHC(O)R₅, -NHC(O)OR₅, -NHC(O)NHR₅, -heterocycloalkyl, -C(S)N(R₅)(R₅), -(C₁-C₁₀)alkylNHC(O)(CH₂)_mR₅, -(C₁-C₁₀)alkylNR₅R₅, -OC(O)(CH₂)_mCHR₅R₅,

-CO₂(CH₂)_mCHR₅R₅, -OC(O)OR₅, -SR₅, -S(O)R₅, -S(O)₂R₅, -S(O)₂NHR₅, and



each R₅ and R₆ is independently selected from -H, -halo, -NO₂, -CN, -OH, -CO₂H, -N(C₁-C₁₀)alkyl(C₁-C₁₀)alkyl, -O(C₁-C₁₀)alkyl, -C(O)(C₁-C₁₀)alkyl, -C(O)NH(CH₂)_m(C₁-C₁₀)alkyl, -OCF₃, -benzyl, substituted benzyl, -CO₂(CH₂)_mCH((C₁-C₁₀)alkyl(C₁-C₁₀)alkyl), -CO₂(C₁-C₁₀)alkyl, -(C₁-C₁₀)alkyl, -(C₂-C₁₀)alkenyl, -(C₂-C₁₀)alkynyl, -(C₃-C₁₀)cycloalkyl, -(C₈-C₁₄)bicycloalkyl, -(C₅-C₁₀)cycloalkenyl, -(C₅)heteroaryl, -(C₆)heteroaryl, -phenyl, naphthyl, -(C₃-C₁₀)heterocycle, -CO₂(CH₂)_m(C₁-C₁₀)alkyl, -CO₂(CH₂)_mH, -NHC(O)(C₁-C₁₀)alkyl, -NHC(O)NH(C₁-C₁₀)alkyl, -NH(aryl), -N=C(aryl), -OC(O)O(C₁-C₁₀)alkyl, and -SO₂NH₂;

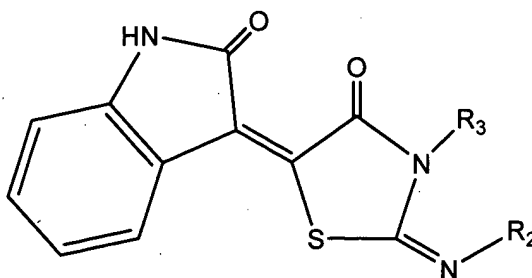
each m is independently an integer ranging from 0 to 8; and

each p is independently an integer ranging from 0 to 5.

34. (New) The method of claim 33, wherein said R₁ is a -(C₅-C₁₀)heteroaryl group.

35. (New) The method of claim 34, wherein said -(C₅-C₁₀)heteroaryl group is a substituted heteroaryl group.

36. (New) The method of claim 35, wherein said compound has the formula:



1 37. (New) The method of claim 36, wherein R_2 is $-S(O)_2R_5$.

1 38. (New) The method of claim 37, wherein R_5 is a



2
1 39. (New) The method of claim 38, wherein said p is 1.

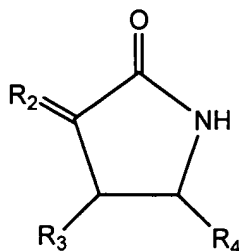
1 40. (New) The method of claim 39, wherein R_6 is a $-(C_1-C_{10})$ alkyl group.

1 41. (New) The method of claim 40, wherein said $-(C_1-C_{10})$ alkyl group is a
2 methyl group.

1 42. (New) The method of claim 41, wherein R_3 is H.

1 43. (New) The method of claim 33, wherein said cancer is selected from the
2 group consisting of ovarian cancer, peritoneal cancer endometrial cancer, cervical cancer, breast
3 cancer, colorectal cancer, uterine cancer, stomach cancer, small intestine cancer, thyroid cancer,
4 lung cancer, kidney cancer, pancreas cancer and prostate cancer.

1 44. (New) A method of treating cancer in a patient comprising:
2 administering to the patient a therapeutically effective amount of a modulator of an Edg-
3 7 receptor wherein the modulator is a compound of Formula (IV):



(IV)

or a pharmaceutically acceptable solvate or hydrate thereof, wherein;

each R_2 , R_3 and R_4 is independently selected from -H, -halo, -NO₂, -CN, -C(R₅)₃,
-(CH₂)_mOH, -N(R₅)(R₅), -O(CH₂)_mR₅, -C(O)R₅, -C(O)NR₅R₅,
-C(O)NH(CH₂)_m(R₅), -OCF₃, -benzyl, -CO₂CH(R₅)(R₅), -(C₁-C₁₀)alkyl,
-(C₂-C₁₀)alkenyl, -(C₂-C₁₀)alkynyl, -(C₃-C₁₀)cycloalkyl, -(C₈-C₁₄)bicycloalkyl,
-(C₅-C₁₀)cycloalkenyl, -(C₅)heteroaryl, -(C₆)heteroaryl, -(C₅-C₁₀)heteroaryl,
-naphthyl, -(C₃-C₁₀)heterocycle, -CO₂(CH₂)_mR₅, -N(OH)aryl, -NHC(O)R₅,
-NHC(O)OR₅, -NHC(O)NHR₅, ~~heterocycloalkyl~~ heterocycloalkyl,
-C(S)N(R₅)(R₅), -(C₁-C₁₀)alkylNHC(O)(CH₂)_mR₅, -(C₁-C₁₀)alkylNR₅R₅,
-OC(O)(CH₂)_mCHR₅R₅, -CO₂(CH₂)_mCHR₅R₅, -OC(O)OR₅, -SR₅, -S(O)R₅,
-S(O)₂R₅, -S(O)₂NHR₅, ~~or~~ and



each R_5 and R_6 is independently selected from -H, -halo, -NO₂, -CN, -OH,
-CO₂H, -N(C₁-C₁₀)alkyl(C₁-C₁₀)alkyl, -O(C₁-C₁₀)alkyl,
-C(O)(C₁-C₁₀)alkyl, -C(O)NH(CH₂)_m(C₁-C₁₀)alkyl, -OCF₃, -benzyl,
-CO₂(CH₂)_mCH((C₁-C₁₀)alkyl(C₁-C₁₀)alkyl), -CO₂(C₁-C₁₀)alkyl,
-(C₁-C₁₀)alkyl, -(C₂-C₁₀)alkenyl, -(C₂-C₁₀)alkynyl, -(C₃-C₁₀)cycloalkyl,
-(C₈-C₁₄)bicycloalkyl, -(C₅-C₁₀)cycloalkenyl, -(C₅)heteroaryl,
-(C₆)heteroaryl, -phenyl, naphthyl, -(C₃-C₁₀)heterocycle,
-CO₂(CH₂)_m(C₁-C₁₀)alkyl, -CO₂(CH₂)_mH, -NHC(O)(C₁-C₁₀)alkyl,
-NHC(O)NH(C₁-C₁₀)alkyl, -NH(aryl), -N=C(aryl),
-OC(O)O(C₁-C₁₀)alkyl, and -SO₂NH₂;

R_2 , R_3 and R_4 taken in any combination can form one or more substituted or unsubstituted
5 or 6 membered cyclic or heterocyclic rings or a 6-membered aromatic ring;
two R_6 groups on adjacent carbon atoms can together form a 5 or 6 membered cyclic or
heterocyclic ring or a 6-membered aromatic ring;

each m is independently an integer ranging from 0 to 8; and

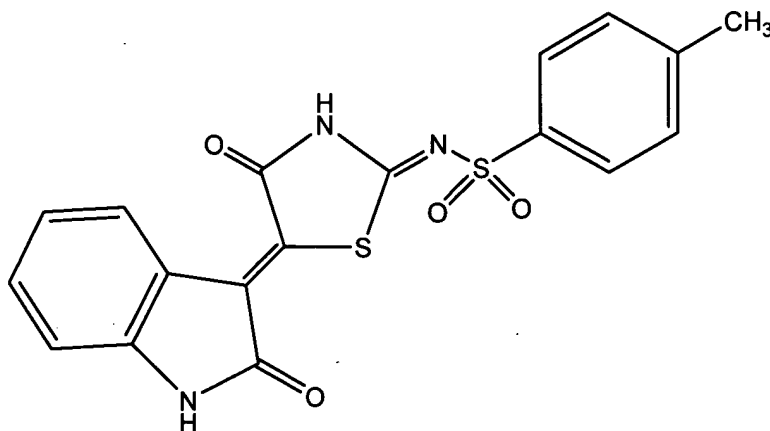
each p is independently an integer ranging from 0 to 5.

45. (New) The method of claim **44**, wherein R₃ and R₄ form a 6-membered aromatic ring.

46. (New) The method of claim **45**, wherein R₂ is a -(C₅-C₁₀)heteroaryl group.

47. (New) The method of claim **46**, wherein said -(C₅-C₁₀)heteroaryl group is a substituted heteroaryl group.

48. (New) The method of claim **47**, wherein said compound has the formula:



49. (New) The method of claim **44**, wherein said cancer is selected from the group consisting of ovarian cancer, peritoneal cancer, endometrial cancer, cervical cancer, breast cancer, colorectal cancer, uterine cancer, stomach cancer, small intestine cancer, thyroid cancer, lung cancer, kidney cancer, pancreas cancer and prostate cancer.